

Health Advisory:

Avian Influenza and the Threat of an Influenza Pandemic

November 15, 2005

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Office of the Director
912 Wildwood
P.O. Box 570

Jefferson City, MO 65102
Telephone: (800) 392-0272

Fax: (573) 751-6041

Web site: <http://www.dhss.mo.gov>

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FROM: JULIA M. ECKSTEIN
DIRECTOR

SUBJECT: Avian Influenza and the Threat of an Influenza Pandemic

Pandemic influenza . . . is an explosive global event in which most, if not all, populations worldwide are at risk for infection and illness. In past pandemics, influenza viruses have spread worldwide within months and are expected to spread even more quickly today given modern travel patterns.

It is the sheer scope of influenza pandemics, with their potential to rapidly spread and overwhelm societies and cause illnesses and deaths among all age groups, which distinguishes pandemic influenza from other emerging infectious disease threats and makes pandemic influenza one of the most feared emerging infectious disease threats.

Although it is unpredictable when the next pandemic will occur and what strain [of influenza virus] may cause it, the continued and expanded spread of a highly pathogenic—and now endemic—avian H5N1 virus across much of eastern Asia, Russia, and eastern Europe represents a significant pandemic threat.

U.S. Department of Health & Human Services Pandemic Influenza Plan, November 2005

There is presently considerable, and justified, concern about the potential for an influenza pandemic, although no one can predict when it will occur and how severe it will be. The purpose of this Health Advisory is to provide information on the current situation with regard to avian H5N1 virus and the possible emergence of a human pandemic, and to present recommendations for medical care providers and facilities, public health agencies, and individuals.

Background and Current Situation

Avian influenza is caused by a number of different influenza A subtype viruses. These viruses occur naturally among wild water birds worldwide. These wild birds carry the viruses in their intestines, but usually do not get sick from them. However, some types of avian influenza are very contagious among birds and infection in domesticated birds such as chickens and turkeys can range from no outward signs to severe respiratory symptoms and death. Infected birds shed influenza virus in their saliva, nasal secretions, and feces. Susceptible birds become infected when they have contact with contaminated excretions or surfaces that are contaminated with excretions. Influenza viruses are identified by a series of letters and numbers and the recent Asian outbreaks involve the influenza A (H5N1) virus – also called “H5N1 virus”. For further information on avian influenza in birds, see <http://www.cfsph.iastate.edu/Factsheets/pdfs/influenza.pdf>. For specific information about the H5N1 avian influenza virus, see <http://www.cdc.gov/flu/avian/gen-info/facts.htm>. For information about avian influenza in poultry, see <http://www.usda.gov/>.

Outbreaks of influenza A (H5N1) virus infections, also known as “avian flu” or “bird flu,” have been reported in various animal populations in several countries throughout Asia, and just recently in Europe. Poultry outbreaks of influenza A (H5N1) occurred in eight countries in Asia (Cambodia, China, Indonesia, Japan, Laos, South Korea, Thailand, and Vietnam) during late 2003 and early 2004. At that time, more than 100 million birds in the affected countries either died from the disease or were killed in order to try to control the outbreak. By March 2004, the outbreak was reported to be under control. Beginning in late June 2004, however, new deadly outbreaks of influenza H5N1 among poultry were reported by several countries in Asia (Cambodia, China, Indonesia, Malaysia Thailand, and Vietnam). These outbreaks appear to be ongoing and have migrated into Russia, Turkey

and Romania. Outbreaks of H5N1 virus infections have been reported in wild birds and other animal species in several countries in Asia, and more recently, in Europe. Moreover, human infections with influenza A (H5N1) have been reported in Thailand, Vietnam, Cambodia and Indonesia. At this time, the World Health Organization (WHO) level of pandemic alert remains unchanged at Phase 3. The current risk to Missourians from the H5N1 avian influenza outbreak in Asia is extremely low. The strain of H5N1 virus found in Asia has not been found in the United States. For further information regarding the phases of a pandemic, go to <http://www.hhs.gov/pandemicflu/plan/pdf/AppC.pdf>.

The Link Between Avian Influenza and a Potential Pandemic

The H5N1 virus does not usually infect humans. In 1997, however, the first case of spread from a bird to a human was seen during an outbreak of H5N1 in poultry in Hong Kong. The virus caused severe respiratory illness in 18 people, 6 of whom died. Since that time, there have been other cases of H5N1 infection among humans. Most recently, human cases of H5N1 infection have occurred in Thailand, Vietnam, Cambodia and Indonesia during large H5N1 outbreaks in poultry. The death rate for these reported cases has been about 50 percent. To date, human infections with avian influenza A viruses detected since 1997 have not resulted in sustained human-to-human transmission, though it does appear that in rare instances infection from person to person occurred among family members with close contact. These rare instances have not changed WHO's overall assessment of the pandemic risk, and it is often impossible to determine if human-to-human transmission occurred since the family members are exposed to the same animal and environmental sources as well as to one another. However, because all influenza viruses have the ability to change, scientists are concerned that the H5N1 virus could undergo further genetic changes and be able to spread easily from one person to another. Because these viruses do not commonly infect humans, there is little or no immune protection against them in the human population. If the H5N1 virus were able to infect people and spread easily from person to person, a worldwide outbreak of influenza (pandemic) could begin. No one can predict when a pandemic, caused by H5N1 or some other novel influenza virus, might occur. However, experts from around the world are watching the H5N1 situation in Asia very closely and are preparing for the possibility that the virus may begin to spread more easily and widely from person to person.

Symptoms of H5N1 Infection in Humans

Influenza viruses are associated with acute, usually self-limited infections, whose symptoms are most commonly fever, muscle aches and pains, and cough. However, illness can be more severe based upon the properties of the virus, the patient's age, pre-existing immunity status, and/or pre-existing medical conditions.

Symptoms of H5N1 in humans have ranged from typical flu-like symptoms (fever, cough, sore throat and muscle aches and pains) to eye infections, pneumonia, severe respiratory diseases (e.g., acute respiratory distress), and other severe and life-threatening complications. The symptoms may vary due to different strains of the virus and routes of exposure.

A recent review article from WHO on avian influenza A (H5N1) infection in humans is available at <http://content.nejm.org/cgi/content/full/353/13/1374>. In addition, the recently released U.S. Department of Health & Human Services (HHS) Pandemic Influenza Plan contains a brief summary of the clinical presentation and complications of illnesses associated with avian influenza A (H5N1) – go to <http://www.hhs.gov/pandemicflu/plan/pdf/S05.pdf> and see pages S5-27 and S5-28.

Surveillance, Diagnostic Testing and Management of Persons Suspected of Being Infected With Influenza A (H5N1)

CDC recommends that state and local health departments, hospitals, and clinicians maintain enhanced surveillance efforts to identify patients at increased risk for avian influenza A (H5N1). Specific recommendations on influenza A (H5N1) testing, and on infection control precautions for persons suspected of having influenza A (H5N1), are available from the Missouri Department of Health and Senior Services (DHSS) at <http://www.dhss.mo.gov/PandemicInfluenza/H5N1Testing-InfectionControl.pdf>. Consultation is also available from DHSS – the primary point of contact for the department is Eddie Hedrick, Emerging Infections

Coordinator. He can be reached at 573-522-8596, or e-mail Eddie.Hedrick@dhss.mo.gov. On evenings, weekends or holidays, call (800) 392-0272. If laboratory testing for avian influenza is being considered, Mr. Hedrick should be contacted before specimens are obtained.

A section of the HHS Pandemic Influenza Plan contains additional recommendations on evaluation and management of persons suspected of being infected with influenza A (H5N1) virus or another novel influenza virus. This section is available at <http://www.hhs.gov/pandemicflu/plan/pdf/S05.pdf>. (Note that Figure 1 on pages S5-16 and S5-17 contains a helpful algorithm summarizing the recommended steps for detection and management of potential cases of influenza A [H5N1] virus infection.)

Exposure routes to the H5N1 virus

Exposure routes to H5N1 are through infected poultry. There are currently no poultry (or any other animals or humans) infected by this virus in the United States. In countries elsewhere in the world with infected poultry, persons who have direct contact with infected poultry and/or surfaces contaminated with bird excretions (e.g., poultry producers, processors and handlers) have a much higher risk because the infected birds shed influenza virus in their saliva, nasal secretions, and feces. Missourians who plan to travel to areas currently impacted by the H5N1 virus and who are concerned about their health can find more information at CDC's Travelers' Website (<http://www.cdc.gov/travel/>).

In an agricultural setting, bird manure containing influenza virus can contaminate dust and soil, causing infection when the contaminated dust is inhaled. Contaminated farm equipment, feed, cages, or shoes can carry the virus from farm to farm. The virus can also be carried on the bodies and feet of animals, such as rodents. The virus can survive, at cool temperatures, in contaminated manure for at least three months. In water, the virus can survive for up to four days at 72° F and more than 30 days at 32° F. Studies have shown that a dime sized amount of contaminated manure can contain enough virus to infect 1 million birds.

In a food handling/preparation setting, there may be some concern that avian influenza could be transmitted from uncooked poultry or poultry products. This is not a health concern in Missouri, as this virus is not found in the United States. Additionally, poultry and poultry products cannot legally be imported from areas known to be affected. In general, poultry and poultry products should be cooked thoroughly before consumption. Care should be taken to wash and disinfect cutting surfaces and utensils, and all persons who handle poultry should wash their hands thoroughly with warm running water and soap immediately after touching raw poultry and before handling other foods or utensils. It should also be noted that, according to WHO, normal cooking (temperatures at or above 70°C) will inactivate the virus. WHO additionally states that, to date, there is no epidemiological evidence that people have been infected through consumption of well-cooked contaminated poultry meat.

Risk of Missourians to H5N1 exposure

The current risk to Missourians from the H5N1 avian influenza outbreak in Asia is extremely low. The strain of H5N1 virus found in Asia has not been found in the United States. However, with the speed of world travel today, it is possible that an infected traveler could return from an affected country to Missouri, and therefore plans are being developed to protect the public health in case such a situation should arise.

Available vaccine and medications for the H5N1 virus

There currently is no available vaccine to protect humans against the H5N1 virus that is being seen in Asia, and most recently in Europe. However, vaccine development efforts are underway. Research studies to test a vaccine to protect humans against H5N1 virus began in April 2005. For more information about the H5N1 vaccine development process, visit the National Institute of Allergy and Infectious Diseases website at <http://www.niaid.nih.gov/publications/flu.htm>. The H5N1 virus currently infecting birds in Asia that has caused human illness and death is resistant to amantadine (Symmetrel) and rimantadine (Flumadine), two antiviral medications commonly used for influenza. Two other antiviral medications, oseltamavir (Tamiflu) and zanamavir (Relenza), may be effective in treating avian influenza caused by the H5N1 virus, though studies still need to be done to document their effectiveness.

Concern about the spread of avian influenza A (H5N1) has caused many individuals to ask their health care providers for prescriptions for oseltamivir. Others have attempted to purchase this drug over the Internet. DHSS does not recommend personal stockpiling of oseltamivir or other antiviral agents (more information is available at <http://www.dhss.mo.gov/PandemicInfluenza/StockpilingFluAntiviralMeds.pdf>).

Likelihood and Effects of Pandemic Influenza

Most experts believe that a pandemic will occur at some time in the future. No one can predict when, where or what virus may cause it. The severity of the next pandemic cannot be predicted, but modeling studies suggest its effect in the United States could be severe. The number of hospitalizations and deaths will depend on the virulence of the pandemic virus. Estimates differ about 10-fold between more and less severe scenarios. Because the virulence of the virus that causes the next pandemic cannot be predicted, two scenarios, based on extrapolation of past pandemic experience, have been developed and are presented in Table 1, which was taken from the HHS Pandemic Influenza Plan (<http://www.hhs.gov/pandemicflu/plan/>).

Table 1. Number of Episodes of Illness, Healthcare Utilization, and Death Associated with Moderate and Severe Pandemic Influenza Scenarios*

Characteristic	Moderate (1958/68-like)	Severe (1918-like)
Illness	90 million (30%)	90 million (30%)
Outpatient medical care	45 million (50%)	45 million (50%)
Hospitalization	865,000	9,900,000
ICU care	128,750	1,485,000
Mechanical ventilation	64,875	742,500
Deaths	209,000	1,903,000

*Estimates based on extrapolation from past pandemics in the United States. Note that these estimates do not include the potential impact of interventions not available during the 20th century pandemics.

Pandemic Preparations in Missouri

Preparations for a possible pandemic, as well as for the emergence of H5N1 infection in waterfowl and poultry in Missouri, are ongoing. Much has been done since 2001 to strengthen the public health system: (e.g. building better communication systems, improving laboratory capacity, strengthening the hospital readiness system, and creating and exercising systems for mass distribution of vaccines or medications). These preparations will be invaluable in a response to a pandemic. In addition, DHSS and many local public health agencies have developed specific plans for pandemic influenza and are working with federal authorities in the development of national policies. Coordination and planning, including exercises, between DHSS, the Missouri Department of Agriculture, other state agencies and the poultry industry continue, with plans in place for the state to respond in the event H5N1 influenza virus enters the United States. Planning will continue at a rapid pace during the coming year as more guidance is expected from the federal level (the federal pandemic influenza plan was released recently and is available at <http://www.hhs.gov/pandemicflu/plan/>), and training sessions and tabletop exercises on pandemic influenza will be taking place around the state.

Even with these preparation measures, it has been 36 years since the last pandemic, and few in the health system today have hands-on experience in working this type of event. Influenza pandemics are different from many of the threats for which public health and the health-care system are currently planning:

- The pandemic will last much longer than most other emergency events and may include “waves” of influenza activity separated by months (in 20th century pandemics, a second wave of influenza activity occurred 3 to 12 months after the first wave).

- The numbers of health-care workers and first responders available to work can be expected to be reduced since they will be at high risk of illness through exposure in the community and in health-care settings, and some may have to miss work to care for ill family members.
- Hospital beds and other medical resources in many locations could be limited because of the numbers of persons affected by the pandemic.

Because of these differences and the expected size of an influenza pandemic, it is important to have completed planning and preparedness activities prior to the event in order to be able to respond promptly and adequately. For this reason, preparations will continue moving forward quickly. DHSS has developed recommended action steps for local public health agencies (<http://www.dhss.mo.gov/PandemicInfluenza/LPHAActionSteps.pdf>) and for individuals (<http://www.dhss.mo.gov/PandemicInfluenza/PersonalActionSteps.pdf>). DHSS has also developed draft isolation and quarantine orders (<http://www.dhss.mo.gov/PandemicInfluenza/DraftOrders.pdf>). A fact sheet on avian influenza and influenza pandemics is available at <http://www.dhss.mo.gov/PandemicInfluenza/FAQs-Avian.pdf>. Finally, DHSS has a pandemic influenza website, which provides access to comprehensive information for medical and public health professionals, and for the public (<http://www.dhss.mo.gov/PandemicInfluenza/>). Further information is provided in the following websites:

- The official U.S. Government website for information on pandemic flu and avian influenza is PandemicFlu.gov, located at <http://www.pandemicflu.gov/>.
- The Centers for Disease Control and Prevention (CDC) avian influenza website is located at <http://www.cdc.gov/flu/avian/index.htm>. **Note that CDC has established avian influenza hotlines: Public 888-246-2675; Spanish 888-246-2857; Clinicians 877-246-4625.**
- The federal government's pandemic influenza plan (HHS Pandemic Influenza Plan) is available at <http://www.hhs.gov/pandemicflu/plan/>.
- A recent review article from WHO on avian influenza A (H5N1) infection in humans is available at <http://content.nejm.org/cgi/content/full/353/13/1374>. An earlier article on avian influenza A (H5N1) in ten patients in Vietnam is available at <http://content.nejm.org/cgi/content/full/350/12/1179>.
- For more information on avian influenza, including a listing of H5 and H7 occurrences in the United States since 1997, visit the Animal and Plant Health Inspection Service website of the U.S. Department of Agriculture (USDA) at <http://www.aphis.usda.gov/>.
- For information on the H7 outbreak in the Netherlands, see: CDC. Human Cases of Avian Influenza A (H7N7) Infection - The Netherlands 2003, at <http://www.cdc.gov/flu/avian/h7n7-netherlands.htm>.
- For more information about the avian influenza outbreak in Asia, visit WHO's Website at http://www.who.int/csr/disease/avian_influenza/en.
- For more information about infection among poultry and animals in Asia, visit the World Organization for Animal Health Web site at http://www.oie.int/eng/en_index.htm.
- For information about food safety issues concerning the avian influenza outbreak in Asia, visit the Food and Agriculture Organization of the United Nations' website at <http://www.fao.org/ag/avian.html>.
- For more information about vaccines and pandemic preparedness, visit HHS' National Vaccine Program Office's website at <http://www.hhs.gov/nvpo/pandemics/> and WHO's pandemic preparedness website at <http://www.who.int/csr/disease/influenza/pandemic/en/>.

CDC's influenza (seasonal, or non-pandemic, influenza) web site is located at <http://www.cdc.gov/flu/>. DHSS influenza website is at <http://www.dhss.mo.gov/Influenza/>.